REMARKS

Applicant notes appreciatively that the previous obviousness rejection based on Brakenhoff *et al.* has been withdrawn. The Examiner now provides an alternative obviousness rejection, still based upon Brakenhoff *et al.*:

I. Claims 7-12, 15-18 and 34-48 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over U.S. Patent No. 5,723,120 (Brakenhoff *et al.*) in view of Doherty *et. al.* (*J. Immunol.*, 149:1666-1670, 1992) and further in view of U.S. Patent No. 5,420,253 to Emery *et. al.*

Applicant cannot agree and responds below.

I. The Claims Are Not Obvious

A. The Proper Standards For A 103 Rejection Have Not Been Used

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference(s) themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20 USPQ.2d 1438 (Fed. Cir. 1991); and *MPEP* § 2142; Establishing A *Prima Facie* Case Of Obviousness. The Examiner is reminded that if ONLY ONE of the above requirements is not met, then a *prima facie* case of obviousness does not exist. The Applicant submits that the Examiner's rejection does not meet these criterion. The Applicant rebuts the establishment of a *prima facie* case of obviousness by the argument below.

1. The Examiner's "Design Choice" Argument Is Flawed

The Examiner has attempted to support the rejection with the assertion that it is merely a "design choice . . . to use either an IL-6 receptor antagonist, or antibodies to IL-6." This is not proper examination. Proper examination requires an evidenciary basis for selecting from the vast number of possibilities. It is not enough for the examiner to simply assert that a particular component might have been selected. Indeed, this approach has been criticized and

rejected by the Board of Patent Appeals and Interferences. In the case of *In re Garrett*, the examiner had stated:

> [W]ear blades having parallel sides are notoriously well known in the prior art and one of ordinary skill in the art would, through routine engineering **design choice**, elect to provide a borehole contacting apparatus with blades having parallel sides.

The Board reversed the obviousness rejection and criticized the examiner for asserting **mere conclusion** rather than reasons for the rejection. *In re Garrett*, (Bd. Pat. Appeals & Interf. 1986), reported in BNA Patent Trademark & Copyright Journal, Vol. 33, Pg. 43, Nov. 13, 1986. The examiner in the present case has made the same mistake as was made by the examiner in the *In re Garrett* case.

2. There Must Be An Evidenciary Basis For The Combination

Applicant submits that the references cannot be considered collectively until the Examiner points to some *evidence* to support combining those references. The purpose behind this requirement is to prevent the Examiner from using the invention itself and hindsight reconstruction to defeat the patentability of the invention. The Federal Circuit has explained this position:

> To prevent the use of hindsight based on the invention to defeat patentability of the invention, this court requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner must show reasons that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed.

See In re Rouffet et al., 149 F.3d 1350, 47 USPQ2d 1453 (Fed. Cir. 1998). It is readily apparent that the law of *In re Rouffet* requires the Examiner to present soundly reasoned arguments based upon the substance of the cited references.[1] Moreover, the law does not regard the Examiner as one skilled in the art. *See In re Rijckaert*, 28 USPQ2d 1955 at 1956 (Fed. Cir. 1993)("[T]he examiner's assumptions do not constitute the disclosure of the prior art."); *See id.* at 1957 ("[W]hen the PTO asserts that there is an explicit or implicit teaching or suggestion in the prior art, it must indicate where such a teaching or suggestion appears."). Indeed, the Federal Circuit has made it clear that "[b]road, conclusory statements regarding

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[1] *Accord Ex parte Clapp*, 227 USPQ 972 (Bd. Pat. App. & Inter. 1985) (stating that the examiner must present convincing line of reasoning supporting rejection).

the teachings of multiple references, standing alone, are not 'evidence.'" *In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614 (Fed. Cir. 1999).

Applicant submits that the Examiner has not provided a sound explanation for combining these references as required by the law in *In re Rouffet*. What the Examiner has provided are unsupported and conclusory statements in a failed attempt to identify the administration of an IL-6 antibody and a TNF antibody composition for the treatment of sepsis. Moreover, the Examiner proceeds from a flawed understanding of the primary reference, *i.e.*, Brakenhoff *et al.*.

B. Brakenhoff *et al.* Does Not Teach The Claimed Antibody Combination

The Examiner makes the following statement:

> In addition, the '120 patent further discloses that other agents which may be combined with IL-6 receptor antagonists include monoclonal antibodies directed to cytokines involved in the sepsis pathway, such as antibodies directed to IL-6, and antibodies directed to TNF (column 12, lines 44-50). *The '120 patent thus teaches that sepsis may be treated by IL-6 activity neutralizing agents, including antibodies to IL-6, and that the treatment of sepsis can be by administration of compositions comprising anti-IL-6 and anti-TNF antibodies.*

(*see* Office Action, p. 3, emphasis added). Applicant has looked carefully at column 12, lines 44-50. In fact, Applicant has read the entire paragraph spanning lines 44 to 59. At no point is there a suggestion of combining anti-TNF antibodies with anti-IL-6 antibodies. Rather, this paragraph teaches that "IL-6 receptor antagonists"[2] can be supplemented with i) antibodies to complement, ii) monoclonal antibody to IL-6, iii) monoclonal antibody to TNF, iv) inhibitors of proteins that cleave the mature TNF, or v) "inhibin." Any one of these is used to supplement the "IL-6 receptor antagonist." The paragraph does not teach combinations[3] of these supplements.[4] Therefore, there is no basis for the Examiner's statement that Brakenhoff *et al.* teaches "compositions comprising anti-IL-6 and anti-TNF-α antibodies."

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[2] This term is defined in the Brakenhoff *et al.* specification so as to include synthetic variants of wild type IL-6.

[3] The Examiner must use only what is actually disclosed in the reference. As the court said in *In re Rosenberger*, "[t]his appears to be an extremely strained interpretation of the reference which could be made only by hindsight." *In re Rosenberger*, 386 F.2d 1015, 1018, 156 USPQ 24, 26 (CCPA 1967).

[4] Moreover, all combinations - whatever they are - are taught to contain an "IL-6 receptor antagonist." Claim 34 (and dependent claims) is directed to an embodiment wherein the formulation only contains (as active ingredients) antibodies to TNF and IL-6.

C. Doherty *et al.* Does Not Teach The Claimed Antibody Combination

A further deficiency of Brakenhoff *et al.* is the failure to even mention IFN antibodies in combination with IL-6 or TNF-α antibodies for treating sepsis. Consequently, the Examiner points to Doherty *et al.* for disclosure of IFN antibody treatment in the presence of TNF-α and their synergistic role(s) regarding LPS-induced sepsis. Doherty *et al.*, however, does not contemplate any combination of IFN-γ antibodies and TNF-α antibodies in the treatment of LPS-induced sepsis. Further, the Examiner fails to take into consideration that Doherty *et al.* is completely silent regarding IL-6 antibodies in the treatment of LPS-induced sepsis.

D. Emery *et al.* Does Not Teach The Claimed Antibody Composition

Finally, the Examiner asserts Emery *et al.* to show a method that extracts IgG antibodies from chicken egg yolks. Emery *et al.* also is of no consequence to the pending independent claims because the reference lacks any teaching for the administration of antibodies to TNF-α, IL-6 or gamma IFN, either singly or in any combination, to mammals for the treatment of sepsis. As such, it adds nothing in combination with the other deficient references.

E. Conclusion

There is no basis for the Examiner's proposed combination of Brakenhoff *et al.*, Doherty *et al.* and Emery *et al.* The Examiner's "design choice" argument is a discredited approach to examination. The Examiner has provided nothing but opinion (made apparently in hindsight using the present specification). This is insufficient to establish a *prima facie* case of obviousness.

Moreover, even if improperly combined, all have a common deficiency. Specifically, none of the references mention a composition comprising an IL-6 antibody and a TNF-α antibody to treat sepsis. This deficiency is a clear failure to establish that the references, in combination, disclose all the limitations of a claim - yet another requirement to establish a *prima facie* case of obviousness.

For the above reasons, the rejection should be withdrawn.

Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicant encourages the Examiner to call the undersigned, collect.

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